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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,402	08/16/2001	Jeffrey L. Browning	B185 US CP DV1	3893

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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT                PAPER NUMBER

1642

DATE MAILED: 03/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/931,402	BROWNING ET AL.
Examiner	Art Unit	
Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 21 February 2002.

2a) This action is **FINAL**.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 7-17,38-49 and 61-70 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 7-17,38-49 and 61-70 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)  The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .	6) <input type="checkbox"/> Other: _____ .

## DETAILED ACTION

1. The examiner of the application has changed. This case has now been transferred as of 2/11/2003. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Christopher Yaen, Group Art Unit 1642.
2. Claims 1-6, 18-37, and 50-60 are canceled without prejudice. Claims 7-17, 38-49, and 61-70 are therefore pending and examined on the record.

### ***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> paragraph***

3. Claims 7-17, 38-49 and 61-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
4. Regarding claims 7-17, 38-49, and 61-70 in the recitation of the phrase "activating agent", it is unclear as to which products or molecules are to be encompassed by the phrase. It is noted that the specification defines the "activating agent" as anything that is able to augment ligand binding to LT-beta-R. However, this is not specifically indicating what type of agent is intended to be within the metes and bounds of the phrase.
5. Regarding claims 7 and dependent claims thereof in the recitation of the terms "reducing", it is a relative term of which there is not reference point from which to gauge a reduction. As such the metes and bounds of the term cannot be determined. With regard to the term "severity", it is a relative term of which there is no reference point to gauge the amount of "severity".

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6. Regarding claims 7 and dependent claims thereof in the recitation of the phrase "effective amount", it is unclear from the specification as to what this amount is intended to encompass. One of skill in the art would not know to what extent to add so as to achieve an effective amount.

7. Claim 8 recites the limitation "LT- $\alpha/\beta$  heteromeric complex" in line 2.

There is insufficient antecedent basis for this limitation in the claim.

8. Claim 17 depends from claims 6-16 of which claim 6 has been canceled, as such it is unclear as to which claims are intended to be included within the limitations of the claim.

9. Claim 49 depends from claims 41-48 of which is a multi-dependent claim. As such the claim is indefinite because it is unclear as to which claim it depends.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph***

10. Claims 7-17, 38-49, and 61-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating colon carcinoma in a host and testing cytotoxic effects of a compound in an in vitro test system comprising the administration of a LT- $\alpha/\beta$  heteromeric complex, a LT- $\beta$ -R activating antibody, selected from BKA11 and CDH10, and IFN- $\gamma$ , and a pharmaceutical composition comprising a LT- $\beta$ -R activating antibody, selected from BKA11 and CDH10, and IFN- $\gamma$  does not reasonably provide enablement for a method of treating neoplasia in general in a subject comprising the administration of any LT- $\beta$ -R activating agents, and a pharmaceutical composition comprising LT- $\beta$ -R activating agents. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to practice and make the invention commensurate in scope with these claims.

The instant specification teaches the ability of an LT- $\alpha/\beta$  heteromeric complex to exhibit cytotoxic effect on tumor cells in the presence of IFN- $\gamma$ . The specification further teaches that such an effect was only observed in the presence of IFN- $\gamma$  suggesting the role of its ability to signal through the TNF family of receptors. The specification further teaches that certain LT- $\beta$ -R antibodies can exhibit activational effects while others can exhibit inhibitory functions. However, nowhere in the specification does it teach any other types of agents that are able to activate LT- $\beta$ -R. Further, the specification has only provided working examples of two specific types of activating antibodies, namely, BKA11 and CDH10, all the other antibodies disclosed are either inhibitory, agonistic/antagonistic or exhibit tumor inhibitory properties independent of the LT- $\alpha/\beta$  heteromeric complex. The specification has also only taught how to use the instant LT- $\beta$ -R activating antibodies in an in vitro test culture system in the form of cytolytic assays and in a SCID mouse model where colon carcinoma cells were injected. Such is not seen as fully enabling for a method of treating neoplasias in general because it is a well accepted fact that the treatment of cancer is often unpredictable and strategies to overcome tumor progression still need to be thoroughly investigated (see Hipp *et al* *in vivo* 2000;14:571-585). There are many obstacles to overcome in the treatment of cancer such obstacles include the ability of the compound to reach the site of the tumor (see Jain *et al* *Cancer and Metastasis Reviews* 1990;9:253-266). Because cancers

are derived from different cell types, they require different modalities of treatment. Surely, the treatment applies for lymphomas or leukemias would not necessarily apply for solid tissue lesions. As such, the specification has only clearly established a method of using specific antagonistic antibodies for the treatment of carcinomas.

### ***Conclusion***

No claim is allowed.

The closest prior art found Hochman PS *et al* (J. Inflamm 1995-1996;46(4):220-34) teaches that the manipulation of the LT/LT-beta-receptor pathway may be a critical pathway for treatment of tumors. Hochman *et al* further discloses that this pathway differs from that of the LT/TNF-receptor pathway in that it initiates a tumoracidal effect without having inflammatory activities.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen  
Art Unit 1642  
March 24, 2003

ANTHONY C. CAPUTA  
SUPERVISORY PATENT EXAMINER  
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